ESTIMATION OF EXPOSURE OF PERSONS IN CALIFORNIA TO PESTICIDE PRODUCTS THAT CONTAIN PROPETAMPHOS

BY

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ABSTRACT

Propetamphos is an organophosphate insecticide that is registered in California primarily for structural pest control. A total of 371 illnesses associated with the use of propetamphos alone or in combination with other pesticides have been reported in California from 1982 to 1993. The reported illnesses were predominantly for non-pesticide handlers, involving mostly office workers, restaurant workers, and residents reentering treated areas. The number of illness reports appears to be in decline since 1988. Propetamphos was extensively absorbed and rapidly eliminated when administered orally to laboratory animals. The major nonconjugated and conjugated metabolites were volatiles consisting of acetone- and acetate-type compounds. In the absence of any dermal absorption data, a dermal absorption rate of 50% was assumed in this document to estimate human absorbed dosage. The workers with potential exposure are the structural pest control operators (PCO) handling propetamphos-containing products. The estimates of absorbed daily dosage (ADD) for PCOs were based on surrogate data and ranged from 13 to 110 µg/kg/day. Occupants and residents entering treated structures could be exposed to propetamphos residues. The estimates of ADD for children and adults reentering a treated resident were 44 and 28 µg/kg/day, respectively.

DPR is currently preparing a risk characterization document for propetamphos because it can cause cholinesterase inhibition in laboratory animals at low dosages. This human exposure assessment document was prepared to be incorporated into the risk characterization document for propetamphos.

Department of Pesticide Regulation
Worker Health and Safety Branch

Human Exposure Assessment

Propetamphos

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INTRODUCTION

Propetamphos is an insecticide that is registered in California mainly for indoor structural uses. It is an organophosphate pesticide that can cause cholinesterase inhibition in mammals. In March 1990, the Department of Pesticide Regulation (DPR) (then a division within the California Department of Food and Agriculture) placed propetamphos into the reevaluation process because of the increasing number of reported illnesses associated with its use. In September of the same year, the DPR requested additional data from the registrant on dermal sensitization, odor threshold, indoor exposure, and dermal absorption. The requested data, except for dermal absorption, have been submitted to the DPR. Propetamphos is on the list of the first 200 pesticides to be reviewed under the Senate Bill 950 (SB 950), the Birth Defect Prevention Act of 1984. The DPR is currently preparing a risk characterization document for propetamphos because animal toxicity studies have shown that it can cause cholinesterase inhibition at low dosages.

Human exposure assessment is essential for the assessment of risk to those that are potentially exposed and is an integral part of the risk assessment process. This human exposure assessment document was prepared to be incorporated into the risk characterization document for propetamphos. It will also serve as a basis for developing mitigation strategies if exposure is found to cause excessive theoretical risk. A propetamphos human exposure study was used to estimate human nonoccupational exposure. Occupational exposure was estimated using propoxur and chlorpyrifos exposure information as surrogates.

CHEMICAL/PHYSICAL PROPERTIES

Propetamphos (CAS # 31218-83-4) is the common name for (E)-1-methylethyl 3-[[(ethylamino) methoxyphos-phinothioyl]oxy]-2-butenoate. The trade name is Safrotin®. Its empirical formula is $C_{10}H_{20}NO_4PS$ with the molecular weight of 281.3. Propetamphos is a light brown, oily liquid that boils at approximately 88 ^{o}C. It is soluble in organic solvents such as xylene, hexane, and acetone. Its water solubility is 110 mg/L at 24 ^{o}C. Its half-life in a buffered aqueous solution is 37 to 47 days at 20 ^{o}C. It photodecomposes in aqueous media with a $t_{1/2}$ of 5 days. It has a vapor pressure of 8.1 x 10^{-5} mm Hg @ 25 ^{o}C (Sandoz, 1978).

FORMULATION AND USAGE

Propetamphos (Safrotin®) is not registered for use on any agricultural commodity nor is it to be used on pets. It is an insecticide currently registered for institutional, industrial, home, and structural uses, both indoors and outdoors. According to the California Pesticide Use Report, 24,235 lb, 23,804 lb, and 38,307 lb of propetamphos were used in 1992, 1993, and 1994, respectively (DPR, 1994; DPR, 1995a; DPR, 1996). The use was almost entirely for structural pest control. Currently, there are two propetamphos-containing products registered in California: one is a pressurized liquid and the other is a liquid concentrate for home and institutional uses. Propetamphos is to be applied as spot, surface, crack & crevice, and injection treatments via low pressure spray. Injection applications are for termites. The application rates are shown in
Table 1.

Table 1: Application Rates for Different Formulations of Propetamphos

Formulation	Application Rate (a.i.)*		
	surface application	spot, crack & crevice	injection
ready-to-use (RTU) aerosol	1%	1%	not on label
liquid concentrate	12.1 - 24.3 μg/cm^2	0.5 - 1.0%	1.0%

* - active ingredient

LABEL PRECAUTIONS

The liquid concentrate formulation contains 18.9% a.i., showing the signal word WARNING on the label with respect to acute oral toxicity. The liquid concentrate formulation is a Toxicity Category III for acute inhalation, acute dermal toxicity and skin and eye irritation (Sandoz Agro, Inc., 1994). The aerosol formulation contains 1% a.i., showing the signal word CAUTION on the label. The aerosol formulation is a Toxicity Category III with respect to acute oral, acute dermal, acute inhalation and skin & eye irritation (Zoecon Corporation, 1989).

No personal protective equipment (PPE) or engineering controls are required or shown on the label for the aerosol or the liquid concentrate formulation.

ILLNESSES/INJURIES

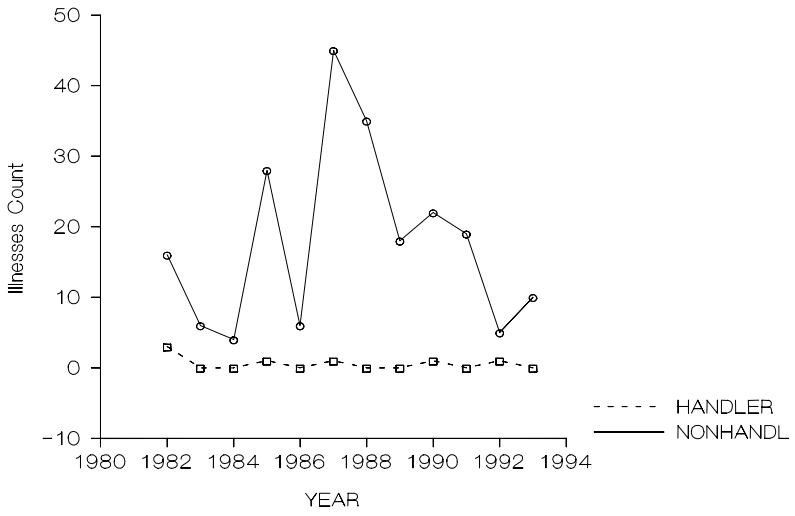
A total of 371 incidents were reported for the 12 year period of 1982 through 1993 (DPR, 1995b). These incidents include illnesses and injuries that were related to the exposure of propetamphos alone or to propetamphos in combination with other pesticides. There was one reported hospitalization and 86 cases involving disability that ranged from 1 to 36 days (DPR, 1995b). The population most adversely affected was the non-pesticide handlers, such as office workers, teachers, restaurant workers, and residents (Fig. 1). Of the 371 cases, 93% (346 cases) were structural residue related (Table 2 & Fig. 1). Twenty-five (7%) of the 371 incidents occurred during application. The most frequent comment given by the injured persons was the detection of an “odor”; and the available cholinesterase data were inconclusive (DPR, 1995b).

Of the non-pesticide handler-related cases due to only propetamphos, 56% (124 cases) were classified as definite/probable systemic incidents and 38% (84 cases) were determined to be possible systemic incidents. Of the residue related cases due to propetamphos plus other pesticides, 56% (84 cases) were classified as definite/probable systemic incidents and 24% (36 cases) were classified as possible systemic incidents. The 12 non-systemic cases were mostly skin-related injuries (9 cases: 4 definite & 5 possible), and the remaining 3 cases involving eye exposure were definite non-systemic.

Of the 25 handler illnesses, only 28% (7 cases) were due to exposure to propetamphos alone while 72% (18 cases) were due to exposure to propetamphos plus other pesticides in the same mix.

Of this 12-year period, illnesses/injuries reported by gender includes only the years 1989 through 1993. During this 5-year period, 164 incidents were reported. Of these 164 incidents, 132 (80%) cases involved adult females. All of the incidents involving adult females were structural residue related. Thirty-two (20%) of the 164 incidents involved males. One of the 32 incidents involved a male child. Of the 31 incidents involving adult males, 21 were structural residue related and 11 occurred during application.

Fig. 1: Reported Illnesses Related to Handler and Non-Pesticide Handler Exposures to Propetamphos: 1982 - 1993.



HANDLER means a person's work tasks require the handling of pesticides.
NONHANDL means non-pesticide handler. Non-pesticide handler means a person's work tasks do not require the handling of pesticides. Such people are office workers, patients, teachers, nurses, *et cetera*.

Table 2: Handler vs. Non-Pesticide Handler Illnesses/Injuries Related to Propetamphos

	Handler[a]			Non-pesticide handler[b]			Total
	systemic[c]	non-systemic[d]	subtotal	systemic[c]	non-systemic[d]	subtotal	
Propetamphos	2	5	7	208	6	214	221
Propetamphos + other pesticides	16	2	18	120	12	132	150
Total			25			346	371

[a] Work tasks requiring the handling of pesticides.
[b] Office workers, patients, teachers, nurses, bar employees, *et cetera*.
[c] Symptoms compatible but may or may not be specific to cholinesterase inhibition.
[d] Eye, skin, or both.

DERMAL SENSITIZATION

No dermal sensitization studies involving human subjects were noted in the public domain literature. The animal model studies indicate the formulated products, up to 75% AI, were not skin sensitizers (Beck, 1984; Braun, 1985; Sandoz Ltd. Agro Development, 1980; Wilkinson and Singer, 1990).

DERMAL ABSORPTION

No dermal absorption data were reported. Worker Health & Safety will evaluate the exposure assessment assuming a 50% dermal absorption (Donahue, 1996).

DISLODGEABLE FOLIAR RESIDUES

Since there are no crop uses, dislodgeable foliar residue is not expected. The presence of dislodgeable residues following indoor structural applications is discussed in the exposure section.

METABOLISM

Female Wistar rats (10/dose) were administered a single oral dose of ^{14}C-labeled propetamphos at 0.6, 6, or 16 mg/kg and placed in metabolism cages for 96 hours while urine and feces were collected (Bhuta, 1979). Additional female rats (4/dose) were placed in metabolism cages for 7 or 48 hours to collect CO_2. The estimates of excretion as $^{14}CO_2$ during the first 7 hours were 80, 60, and 40% at 0.6, 6, and 16 mg/kg, respectively. Approximately 12, 20, and 38% of the radioactivity was excreted in the urine at the respective dosages. Fecal excretion was less than 3% of the administered dose. Greater than 95% of the administered dose was excreted within

the first 24 hours, indicating that when administered orally, propetamphos is extensively absorbed and rapidly eliminated.

In the same study (Bhuta, 1979), another three female rats/time/dose were administered labeled propetamphos at 0.6 and 6 mg/kg and were sacrificed at 1, 2, 4, 8, 24, 72, or 96 hours for blood and tissue distribution analyses. At 0.6 mg/kg dose, the radioactivity in blood showed a monophasic elimination pattern with an estimated half-life of 60 hours. At 6 mg/kg dose, the elimination followed a biphasic pattern with estimated half-lives of 12 and 110 hours. The investigator suggested that these long half-lives do not indicate bioaccumulation but rather reflect the distribution and incorporation of the radiolabeled metabolites into natural constituents in tissues through the carbon pool. Blood and tissue radioactivity analyses within one hour of administration showed that the blood levels were lower than most surrounding tissues. The bone marrow and reproductive organs had the highest levels. In a separate study, when rats were given multiple oral doses, the highest tissue levels were in the lung, skin, and fat (Patel, *et al*., 1982). The investigators suggested that the difference in the tissue residues with single and multiple doses may be due to an increased metabolism rate in the steady state condition.

The analysis of urine collected by Bhuta (1979) showed that the major non-conjugated and conjugated metabolites were volatiles consisting of acetone- and acetate-type compounds (Patel and Winkler, 1982). Minor non-volatile metabolites were desmethyl, desisopropyl, and desmethyl-desisopropyl propetamphos. The investigators proposed that propetamphos is metabolized by hydrolytic reactions, breaking the P-O-vinyl bond to form an acetoacetate moiety which decarboxylates to acetone and CO_2 after ester hydrolysis.

HUMAN EXPOSURE

Propetamphos uses are limited to indoor structural pest control in California. The workers with potential exposure are the structural pest control operators (PCO) handling the product. The exposure to individuals applying propetamphos in homes and institutions is shorter in duration and frequency when compared to PCOs. Occupants and residents entering treated structures could be exposed to propetamphos residues. Children and adults of residential structures who spend much of their time indoors and have movements that result in greater contact with treated areas may be the subgroup with the greatest potential of exposure to residues.

Worker Exposure (Mixer/Loader/Applicator for Indoor Applications)

There are no studies available that monitored the exposure of structural pest control operators during indoor application of propetamphos to carpets. Pesticide handlers exposure database (PHED) may not be an ideal surrogate to estimate the exposure of PCOs or others workers handling propetamphos for indoor home use. The closest exposure data in the PHED are greenhouse applicators, farm house applicators, and painters. The estimates of exposure of propoxur applicators were used as surrogate to estimate the exposure of applicators using identical or similar formulations of propetamphos. In the DPR exposure assessment document for propoxur, four propoxur exposure monitoring studies were reviewed (Sanborn, 1995). The estimates of exposure were made for applicators using an aerosol (1%), a bait (2%), a ready-to-

use spray (0.95%), and a 1% spray mix prepared from a wettable powder formulation. The percent of a.i. in the aerosol and ready-to-use formulations are identical to those of propetamphos. The exposure information for these two formulations was used as surrogate data for propetamphos. There are no wettable powder or bait formulations of propetamphos. Propoxur applicators wore cotton coveralls, baseball caps and chemical resistant gloves in addition to or in place of normal work clothing (long-sleeved shirt, long pants). Dermal exposure was monitored using patch dosimetry according to Durham and Wolfe (1962). Dermal exposure was calculated using patches attached under a layer of clothing. Hand washes were collected to estimate the exposure to hands. Inhalation exposure was monitored by collecting air samples from the breathing areas of applicators, using personal air pumps equipped with quartz microfiber air filters. More than 80% of the patches were below the limit of detection for applicators using the aerosol, bait, and ready-to-use formulations. In estimating the exposure, samples below the limit of detection were assumed to contain residues at one-half of the limit of detection. The estimates of absorbed daily dosage (ADD) and annual average daily dosage (AADD) of propetamphos applicators using aerosol or ready-to-use formulations are provided in Table 3.

Table 3: Estimate of ADD and AADD for Applicators Handling Different Formulations of Propetamphos Based on Surrogate Data

Formulation (n)	Dermal exposure (ug/application)	Inhalation exposure (ug/application)	Duration of application (hour)	ADD[a] (ug/kg/day)	AADD[b] (ug/kg/day)
1% aerosol (32)	390 (2.1)*	40 (2.0)*	0.41	13.8	8.8
1% RTU trigger pump spray (32)	260 (1.8)*	2 (1.8)*	0.27	12.8	8.2
1% E.C. mix for soil injection (8)	16500**	130**	2.8	109.6[c]	69.9

a - Based on dermal absorption of 50% (see dermal absorption section), inhalation uptake of 50% (Raabe, 1988), adjusted for 2 hours of actual application time and male body weight of 75.9 kg (Thongsinthusak, *et al*., 1993a). The propetamphos product labels have no specific PPE statements. Workers were assumed to wear work clothing and gloves based on dermal hazards shown on the product labels and as a common practice.

b - An average of 233 days of work per year (Munro, 1992).

c - PCOs worked an average of 7 hours per day, 2.8 hours of actual application and the rest for site preparation.

* - Geometric mean (geometric standard deviation) adapted from Sanborn, 1995.

** - Arithmetic mean adapted from Thongsinthusak *et al*., 1993.

(n) = number of replicates

RTU - Ready-to-use

In the chlorpyrifos exposure assessment document, an estimate of exposure of PCOs using chlorpyrifos for termite control was made based on an exposure study that monitored dermal and inhalation exposure of PCOs during chlorpyrifos sub-slab and soil injection (Thongsinthusak, *et al*., 1993). This estimate of exposure was used as a surrogate to estimate the exposure of applicators using propetamphos for the same purpose. An emulsifiable concentrate formulation of chlorpyrifos was mixed with water to make a 1% solution. Dermal exposure was measured using gauze patches and hand washes. Patches were placed outside the work clothing at the neck,

chest and both shoulders to measure exposure to the head and neck. Additional patches were placed underneath the work clothing at the forearms, and upper and lower legs to measure exposure to protected areas of the body. The exposure to torso was estimated using patches placed outside the work clothing and assuming the work clothing provided 90% exposure protection. Inhalation exposure was determined using personal air pumps equipped with glass fiber filters. The PPE worn by the workers was not standardized and workers did not wear gloves during most of the work period. Six of the eight workers rolled up their sleeves, exposing the forearm patches. Most of the exposure occurred to upper and lower legs (51%) and forearms (34%). The estimate of exposure of applicators applying propetamphos as soil injection for termite control is also shown in Table 3.

Residential Exposure

Since the predominant use of propetamphos is for indoor structural pest control, there is a potential for exposure of occupants entering treated structures. The potential exposure of residents, particularly children, entering treated homes is a primary concern since they spend more time indoors and, therefore, have the greatest potential exposure. In order to evaluate the indoor exposure of residents, a study was conducted to monitor the potential dermal and inhalation exposure of human volunteers entering carpeted rooms treated with propetamphos (Rosenheck and Hudlow, 1993). The study was conducted in February of 1993 in Fresno, using vacated and cleaned hotel rooms. The study was conducted in compliance with the US EPA Good Laboratory Practice standards except for collection, handling, and analysis of blood cholinesterase samples.

A 0.5 percent propetamphos solution was applied to the 100 percent nylon carpet at the label-recommended rate of one gallon of product per 1,500 square feet by a licensed PCO as a broadcast spray. The exposure of five human volunteers (2 males, 3 females) was monitored at 3, 6, and 9 hours after application. The volunteers wore a full-body dermal dosimeter (long underwear, athletic socks, and gloves, all made of 100 percent cotton) and entered hotel rooms treated with propetamphos at the above intervals. Two rooms were used for each reentry interval resulting in ten replicates for each reentry interval. The volunteers performed a set of Jazzercise® routines in each room for approximately 20 minutes. The Jazzercise® routines allowed maximum body contact with the treated carpet. Face and neck wipes were collected to estimate dermal exposure to uncovered areas of the body. Hand rinses were collected in 300 mL of a 0.01 percent v/v sodium dioctyl sulfosuccinate solution to remove any residues that may have passed through the gloves. Full-body dosimeters were cut into three sections (arms, upper body, lower body) after collection. Inhalation exposures for children and adults were estimated from propetamphos residues in the air samples taken from the center of each room at the height of 6 and 36 inches, respectively.

Air samples were taken at the rate of 1.5 liter/minute using a cassette equipped with a glass fiber filter (1 μm pore size) and polyurethane foam plug. Air sampling began when the volunteers entered the room and continued for approximately 4 hours. Dislodgeable residue samples were collected at each reentry interval by rolling a swivel handled roller weighing 17 kg over four 0.165 m^2 cotton cloths. The roller moved back and forth ten times over the cloth that was placed over the treated carpet. The level of propetamphos applied to the carpet was determined by

analysis of four 0.165 m^2 cotton cloth samples with impervious backing that were placed in each room prior to application and were collected 15 minutes after application. The level of residues on the carpet was also determined by theoretical calculation of the amount of product sprayed in each room.

All collected samples were stored on dry ice in an ice chest. Samples were delivered the next day to a walk-in freezer until transported to the analytical laboratory five days later where they were kept at or below 0°C until analysis. Spike and control samples were taken on the day of monitoring in the same hotel but in separate rooms. Two samples of each matrix were spiked, one at 5.1 µg/matrix and the other at 102 µg/matrix. All spiked matrices except for face and neck wipes, hand wash solutions, and air samples, were kept exposed to the environment for 20 minutes before storage in an ice chest containing dry ice. Air samples remained exposed to the environment for 40 minutes. Average field recovery for all matrices ranged from 75 percent (hand washes) to 89 percent (full-body dosimeters). Samples below the minimum quantifiable level (MQL) were assumed to contain residues half the MQL. These samples were not corrected for field recoveries. All other samples were corrected for average field recovery for that specific matrix.

Table 4. Total and Dislodgeable Residues of Propetamphos on the Carpet and Air Residues Following Carpet Treatment

Post application reentry (hours)	Total carpet residue (µg/cm^2)	Dislodgeable residue (roller) (µg/cm^2)	Transfer to roller (%)	Air residue at 6 inches (µg/m^3)	Air residue at 36 inches (µg/m^3)
3	16.3	0.079	0.49	6.05	8.41
6	21.1	0.074	0.35	6.36	6.88
9	17.2	0.112	0.65	9.83	12.90
Average	18.2	0.088	0.50	7.41	9.73

The amount of a.i. used in each room was approximately 2.9 grams. The calculated target value for total deposition on each cloth was 23.0 mg/cloth or 13.9 µg/cm^2. The actual level of total residues on the deposition cloths that were placed on the carpet prior to application was between 99 and 162% of the calculated value. The mean residue found on the carpet was 30.0 mg/cloth or 18.2 µg/cm^2.

Plasma and RBC cholinesterase levels of volunteers were determined before and after the exposure. Volunteers were observed up to two weeks following the exposure. None exhibited any symptoms of discomfort or toxicity. Their cholinesterase levels tested 24 and 72 hours after the exposure remained within ±15 percent of the pre-exposure range.

Table 5. Dermal Exposure of Volunteers Performing Jazzercise® on Carpets Treated with Propetamphos

Reentry post application (hours)	Duration of Exposure (hour)	Head exposure (µg/person)	Body exposure (µg/person)	Hand exposure (µg/person)	Dermal exposure (µg/person/ 0.33 hour)	Dermal Exposure (µg/person/ hour)
3	0.308	1.3	979	162	1,143	3,711
6	0.275	1.2	768	140	909	3,305
9	0.308	1.0	1,188	183	1,371	4,451
Average	0.297	1.2	978	162	1,141	3,822
% of total		0.10	85.7	14.2	100	

Dermal exposure to head, body, and hands of volunteers at various times of reentry is shown in Table 5. The daily exposure to residents reentering a house three hours after propetamphos application was estimated with the following assumptions: occupants with no clothing, one hour of extensive dermal contact (Jazzercise®) with the treated area would provide as much dermal contact as a daily normal activity, and 6 hours of activity and 18 hours of rest for inhalation exposure. Daily dermal exposure was calculated as follows:

Daily dermal exposure:
Adults = (3,822 µg/person/day)/70.9 kg = 53.9 µg/kg/day
Children = [(3,822 µg/person/day) x (3,925 cm^2/17,900 cm^2)]/10.5 kg = 79.8 µg/kg/day

Based on adult body weight of the study participants, adult body surface area from Thongsinthusak, *et al*., 1993a (average of 2 males and 3 females), and child body surface area and body weight from Snyder, *et al*., 1974.

Oral exposure was estimated as a fraction of hand exposure, assuming 5% and 50% of hand exposure would be ingested by adults and children, respectively (Ross, et al., 1992). Since hand exposure constituted 14% of total dermal exposure (Table 5), oral exposure was estimated as follows:

Daily oral exposure:
Adults = (53.9 µg/kg/day x 14%) x 5% = 0.4 µg/kg/day
Children = (79.8 µg/kg/day x 14%) x 50% = 5.6 µg/kg/day

The estimates of ADD for indoor occupants are shown in Table 6. Since the oral contribution is derived from the total dermal exposure, dermal exposure in Table 6 was corrected for the fraction of hand exposure that will be ingested.

Table 6. Estimates of ADD and AADD for Occupants Entering Carpeted Rooms Treated with Propetamphos

Indoor Occupant	Body weight (kg)	Inhalation rate (m^3/hour)		Exposure (µg/kg/day)			ADD[d] (µg/kg/day)	AADD[e] (µg/kg/day)
		activity	rest	Dermal	Oral	Inhalation[c]	Total	Total
Adult[a]	70.9	0.66	0.50	53.5	0.4	2.2	28.3	9.3
Child[b]	10.5	0.25	0.09	74.2	5.6	2.6	44.0	14.5

a - Inhalation rates from Thongsinthusak, *et al*., 1993a (weighted average for 3 female and 2 male study participants). Average body weight of the study participants.

b - Body weight, body surface area, and inhalation rates from Snyder, *et al*., 1974.

c - The first 6 hours of exposure is based on average of 3 to 9 hours post-application air residues measured at 6 and 36 inches for children and adults, respectively, and the last 18 hours of exposure is based on 9 hours post-application air residues at 6 and 36 inches for children and adults, respectively.

d - Based on dermal absorption of 50% (see dermal absorption section), inhalation uptake of 50% (Raabe, 1988), and oral absorption of 100%.

e - A total of 24 applications in a year as label recommends bimonthly maintenance, and 5 days of exposure following each application.

Based on an equilibrium model, the dislodgeable residue data collected by the roller can also be used to estimate dermal exposure. This model assumes that during the period of contact of the body with the treated surface, the concentration on the body will come into equilibrium with the dislodgeable residue concentration on the surface. It also assumes that the total human body surface area will come in contact with the treated carpet. Therefore, the exposure to the skin surface area in contact with the treated carpet will be equivalent to the residues found in sampling cotton cloths pressed against the treated carpet (dislodgeable residues). Table 7 shows dermal exposure estimates based on dislodgeable residue rate of 0.088 µg/cm^2, using the equilibrium model. Inhalation exposure was assumed to be the same as shown in Table 6. Oral exposure was calculated the same manner as was described previously.

Table 7. Estimate of ADD and AADD Based on Equilibrium Model for Occupants Entering Carpeted Rooms Treated with Propetamphos

Indoor Occupant	Body weight (kg)	Body surface area (cm^2)	Dislodgeable residues (µg/cm^2)	Exposure (µg/kg/day)			ADD[b] (µg/kg/day)	AADD[c] (µg/kg/day)
				Dermal	Oral	Inhalation[a]	Total	
Adult	70.9	17,900	0.088	22.0	0.2	2.2	12.3	4.0
Child	10.5	3,925	0.088	30.6	2.3	2.6	18.9	6.2

a - From Table 6.

b - Based on dermal absorption of 50% (see dermal absorption section), inhalation uptake of 50% (Raabe, 1988), and oral absorption of 100%.

c - A total of 24 applications in a year as label recommends bimonthly maintenance, and 5 days of exposure following each application.

This study indicates that dermal exposure was the primary route of exposure and occurred mainly to upper and lower parts of the body. Hand exposure, which includes the oral exposure, accounted for 14.2% of the total dermal exposure. Exposure to the head was minor. The roller method indicated that only 0.5% of residues on the carpet is dislodgeable (Table 4). Based on the dislodgeable residue values in Table 4 and dermal exposure values in Table 5, an average dermal transfer factor of 43,800 cm^2/ hour can be obtained. None of the actual carpet residues, dislodgeable residues, or dermal exposure values shown in Tables 4 and 5 exhibit a declining pattern over the time period of monitoring. This is consistent with a propetamphos dislodgeability study, indicating almost no residue dissipation over four weeks following the application (Zoecon, 1988). In this study, however, dislodgeable residues showed a slow and gradual decline over the same period, indicating approximately 50% decline in 5 days. Assuming that the exposure would decline parallel to the reduction in dislodgeable residues, the AADD in Tables 6 and 7 were calculated based on average 5 days of exposure after each application and two applications each month.

EXPOSURE APPRAISAL

The science of risk assessment is filled with uncertainty, and the risk assessor tends to be very conservative when making the numerous assumptions that are inherent in the process. It is incumbent upon the risk assessor to openly and honestly discuss the sources of uncertainty so that the risk manager can put them in perspective. The best risk estimates are made with adequate high quality data. Unfortunately, for many chemicals such data are lacking.

There are several factors in most exposure assessments that make them very conservative. Even with "reasonable" input parameters for exposure calculation, there is a high degree of conservatism (tendency to overestimate exposure) not immediately apparent. These factors are very real, but typically hidden and therefore not acknowledged. Below is a brief narrative on the most important factors that produce overestimates.

Dermal versus Oral Plasma Levels

Dosage is expressed as a single static value both in worker exposure and animal toxicology studies. The rate of dermal absorption is always lower than the rate of oral absorption in animals used for toxicology testing. Adverse effects occur when plasma levels in the target organ exceed a critical level. However, dermal acquisition occurs over the entire workday, and because dermal absorption is slower than oral, plasma levels for the same total absorbed dosage will not be nearly as high for a dermal versus oral exposure. A dermal dose acquired over the entire workday produces peak plasma levels much lower than the bolus oral feeding dosage acquired by animals in seconds to minutes. Because the effect is highly dependent on plasma level, treating an eight-hour dermal acquisition as a bolus is so conservative that it outweighs any other perceived source of underestimating exposure. The net effect of assuming instantaneous dermal dose acquisition and absorption is an overestimate of peak plasma concentration compared to the oral route by several fold for the same absorbed dose (Table 8). Note that the lower the dose, the more pronounced this difference becomes. This difference is particularly pertinent when comparing the doses used in a toxicology study to those to which a human would be exposed.

Table 8. Peak Plasma Levels in Man After Oral and Dermal Exposure to Fluazifop-Butyl[a], Normalized for Total Absorbed Dose

Applied Dose (mg)	Route of Exposure	Absorption (% of Applied)[b]	Peak Level (µg/L/mg)[c]	Ratio of Levels Oral vs. Dermal
6.1	oral	100.0	100.0 (3 h)	-
200.0	dermal	1.5	73.3 (22 h)	1.4
20.0	dermal	3.4	32.4 (22 h)	3.1
2.0	dermal	8.0	12.5 (22 h)	8.0

[a] adapted from Auton *et al*. (1993).

[b] *in vivo* absorption as measured by Auton *et al*. (1993), except for oral; note that the peak plasma concentration ratios between dermal and oral administration would have been (proportionally) higher, if a value lower than the default of 100% were used for oral absorption of this pesticide.

[c] normalized for total absorbed dose; in parentheses are the intervals between the time of dosing and the time at which the peak plasma level occurred.

Lower urinary metabolite concentrations (an indication of lower peak plasma concentrations) are also seen with dermally applied pesticides when compared with the urinary metabolite concentration observed following oral dosing (Krieger *et al*., 1993).

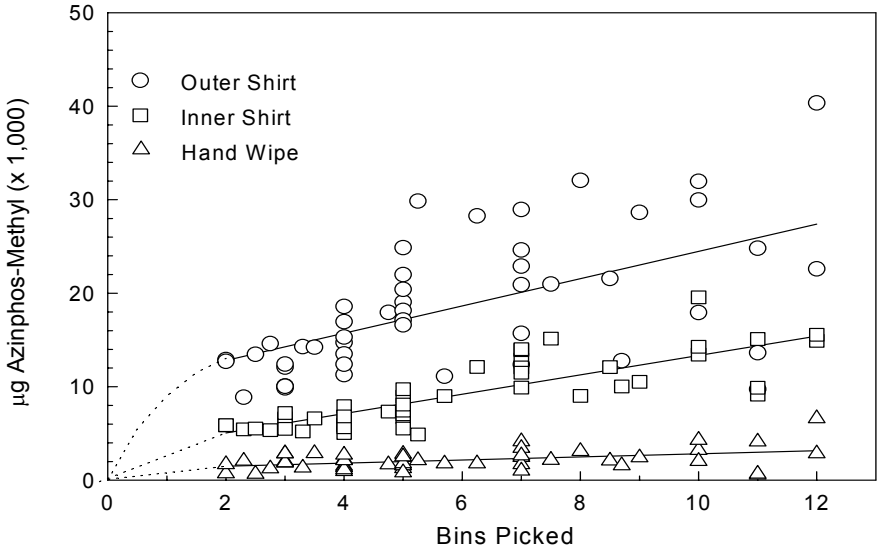
Short Workday Exposure Monitoring Overestimates Full Day

Another source of overestimated dose comes from partial-day monitoring. Figure 2 shows that if an estimate of full-day exposure were extrapolated from 1/3 day (four bins picked) the exposure would be overestimated by more than 50 - 80% and from 1/2 day (six bins picked) 20 - 40%. Shorter monitoring periods are encouraged because it allows an investigator to obtain two or more replicates per individual per day of monitoring. Note that hand residues remain virtually constant indicating that they rapidly come into equilibrium with their environment. Thus summing hand washes taken throughout the day grossly overestimates actual dose. This same principle is operative for pesticide handler exposure monitoring studies.

Conclusion About Exposure Estimates

These factors are operating in the vast majority of exposure estimates and because they are multiplicative, result in overestimates of several fold. The concern that the maximally exposed individual is not adequately represented by mean estimates of exposure is not well founded when considering all the "hidden" conservatism built into all estimates of exposure resulting from the dermal route.

Figure 2. Dermal Monitoring Residues vs. Peach Production, Sutter County, 1989[a]



[a] adapted from Spencer *et al*. (1995).

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